Chemistry of Heterocyclic Compounds, Vol. 34, No. 2, 1998

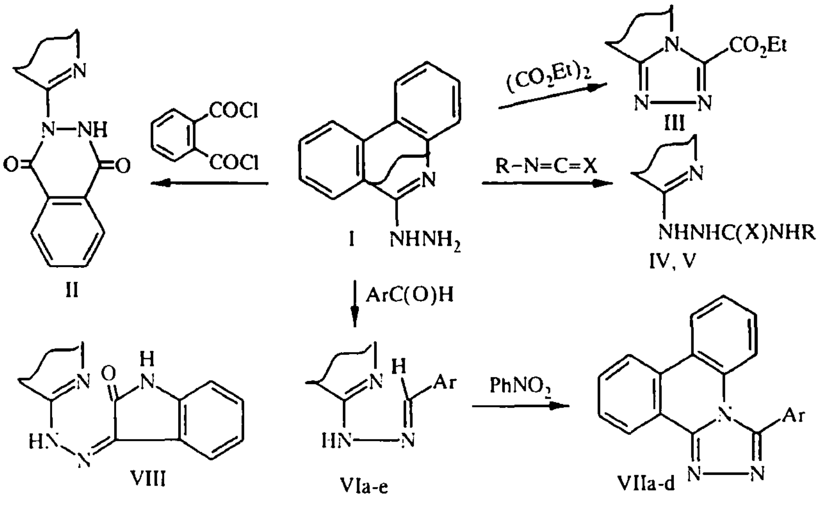
STUDY OF 6-HYDRAZINOPHENANTHRIDINE IN ACYLATION AND ANNELATION REACTIONS OF THE 1,2,4-TRIAZOLE RING

A. G. Mikhailovskii

The reactions of 6-hydrazinophenanthridine with phthaloyl chloride and isocyanates occur at the hydrazo group. Acylation of this hydrazidine by diethyloxalate or oxidation of the hydrazones obtained from it lead to annelated 1,2,4-triazoles.

One of the most interesting reactions of α-hydrazine-substituted pyridines and their analogs and also their derivatives (hydrazides and hydrazones) is annelation of the 1,2,4-triazole ring. The 1,2,4-triazoles formed in this case are promising as synthons and biologically active compounds [1, 2]. Earlier we obtained 6-hydrazinophenanthridine and studied some of its chemical properties [3, 4] and its biological activity [5-7]. Practically no other data is available in the literature on the properties of derivatives of this hydrazidine. The goal of this work was to study this reagent in acylation and annelation reactions of the 1,2,4-triazole ring.

The investigations showed that compound I easily enters into various acylation reactions. Thus the reaction of this compound with phthaloyl chloride yields the phthalazine derivative II. Boiling hydrazidine I in excess diethyloxalate leads to the annelated 1,2,4-triazole III. Treatment of compound I with *p*-tolylisocyanate or allylisothiocyanate leads to respectively compounds IV and V. The hydrazones VIa-e, VIII are the products of reaction of hydrazidine I with aromatic aldehydes [3] and isatin. Simple boiling of hydrazones VIa-d in nitrobenzene leads to the corresponding 1,2,4-triazoles VIIa-d.



IV R = C_6H_4Me-*p*, X = O; V R = $CH_2CH = CH_2$, X = S; VI, VII a Ar = Ph, b $C_6H_4NO_2$-*p*, c $C_6H_4NO_2$-*m*, d C_6H_3-3,4-$CH_2(O)_2$; VI e Ar = C_6H_3-3,4-$(OH)_2$

Institute of Technical Chemistry, Urals Branch, Russian Academy of Sciences, Perm' 614000, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 186-189, February, 1998. Original article submitted July 3, 1997.

TABLE 1. Characteristics of Compounds II-IX

Compound	Empirical formula	Found % Calculated %: C	H	N	mp, °C	IR spectrum, cm^{-1}: C=O, C=N	NH, OH	PMR spectrum, δ, ppm	Yield, %
II	$C_{21}H_{13}N_3O_2$	74,1 74,3	3,7 3,9	12,2 12,4	320 (decomp.)	1680	3340	6,83 - 8,80 m(12H, Ar); 10,40 s (NH)	88
III	$C_{17}H_{13}N_3O_2$	70,0 70,1	4,4 4,5	14,5 14,4	156...157	1730	–	1,50 t ($C\underline{H}_3CH_2$); 4,56 q ($CH_3C\underline{H}_2$); 7,45 - 8,79 m (8H, Ar)	53
IV	$C_{21}H_{20}N_4O$	73,0 73,2	5,8 5,9	16,1 16,3	315 (decomp.)	1650	3220, 3310, 3350	2,15 s (3H, CH_3); 6,20, 8,40 and 9,83 (3NH); 6,73 - 8,0 m(12H, Ar)	72
V[*2]	$C_{17}H_{16}N_4S$	66,1 66,2	5,1 5,2	18,3 18,2	290 (decomp.)	–	3280, 3310, 3360	4,13 m (CH_2N); 5,06 m (H_2C=); 5,67 m (-HC=); 7,16 - 9,0 m (12H, Ar and NH); 10,0 (NH)	57
VIa	$C_{20}H_{15}N_3$	80,6 80,8	5,0 5,1	14,2 14,1	146...148	1625	3100	7,0 - 8,33 m(13H, Ar and NH)	61
VIc	$C_{20}H_{14}N_4O_2$	70,1 70,2	4,1 4,1	16,3 16,4	248...249	1625	3100	6,80 - 8,70 m (12H, Ar and NH); 8,70 s (HC=);	86
VId	$C_{21}H_{15}N_3O_2$	73,7 73,9	4,2 4,4	12,1 12,3	253...254	1625	3090	6,05 s (OCH_2O); 6,99 - 8,43 m (11H, Ar and NH); 8,38 s (HC=)	76
VIe	$C_{20}H_{15}N_3O_2$	72,7 72,9	4,5 4,6	12,9 12,8	240 (decomp.)	1625	3100, 3400	6,70 - 8,57 m(11H, Ar and NH); 8,70 s(HC=); 10,73 s and 10,78 s (20H)	67
VIIa	$C_{20}H_{13}N_3$	81,2 81,3	4,2 4,4	14,3 14,2	146...148	–	–	7,10 - 8,63 m (13H, Ar)	71
VIIb	$C_{20}H_{12}N_4O_2$	70,5 70,6	3,5 3,6	16,6 16,5	250 (decomp.)	–	–	7,0 - 8,65 m(12H, Ar)	90
VIIc	$C_{20}H_{12}N_4O_2$	70,4 70,6	3,4 3,6	16,4 16,5	245...246	–	–	7,15 - 8,70 m (12H, Ar)	87
VIId	$C_{21}H_{13}N_3O_2$	74,2 74,3	3,8 3,9	12,5 12,4	256 (decomp.)	–	–	6,05 s (OCH_2O); 6,99 - 8,43 m(11H, Ar)	92
VIII	$C_{21}H_{13}N_4O$	74,7 74,8	3,8 3,9	16,7 16,6	291...292	1620, 1610	3230, 3310	6,70 - 8,84 m(12H, Ar); 10,52 s and 11.50 s (2NH)	86

---

*The compounds were recrystallized from benzene (VIc, VIIb), dioxane (V), DMF (II, VId, VIId), AcOH (IV, VIIc), and isopropyl alcohol (all the rest).

[*2] Found, %: S 10.4. Calculated, %: S 10.2.

Study of the possibility of further conversions of compound VIII showed that when it is boiled in xylene with addition of TsOH or in acetic acid (monitored by TLC), no changes occur.

Compounds II-V are colorless crystalline high-melting materials (see Table 1), difficultly soluble in most organic solvents. The hydrazones VIa-e have a characteristic yellow color, which becomes less bright after oxidation to triazoles. Hydrazone VIII retains its bright-red color, characteristic of isatin.

The spectral characteristics of the new compounds are presented in Table 1. In the PMR spectrum of the lactam II, we observe a singlet from the NH group (10.40 ppm), and in the IR spectrum of this compound we see absorption bands in the 1680 cm^{-1} (C=O) and NH (3340 cm^{-1}) regions. The structure of triazole III has been proven by the presence in the PMR spectrum of signals from the ethyl group, the complete disappearance of signals from the protons of the NH groups (6.10 ppm [3]), the absence of the corresponding bands in the IR spectrum, and in addition by the presence in the IR spectrum of an ester carbonyl band (1730 cm^{-1}). In the PMR spectrum of compound IV, we observe all three singlets from the NH groups, and one of them (6.20 ppm) is located close to the analogous signal from the NH group of the starting hydrazidine I. This provides a basis for hypothesizing that it is specifically the terminal NH_2 group which is involved in the acylation. A similar pattern is seen in the spectrum of compound V, which is a thiosemicarbazide derivative. In the IR spectra of compounds IV and V, there are absorption bands for all three NH groups.

The spectra of the synthesized hydrazones VIa, c-e are similar to the spectra of previously obtained compounds in this series [3]. The PMR spectrum of compound VIe contains two singlets from the OH groups (10.73 and 10.78 ppm). In the IR spectrum of this compound, there is an absorption band from the OH group (3400 cm^{-1}). In the PMR spectra of triazoles VIIa-d, in contrast to the spectra of the starting hydrazones, we see no singlet from the azomethine proton in the 8.38-8.78 ppm region. This is the main indication allowing us to conclude that they have a tetracyclic structure.

EXPERIMENTAL

The PMR spectra were recorded on an RYa-2310 spectrometer (60 MHz) in DMSO-D_6, except for compound III whose spectrum was taken in $CDCl_3$; internal standard, HMDS. The IR spectra were obtained on a UR-20 in Vaseline oil. TLC was done on Silufol UV-254 plates in the system acetone–ethanol–chloroform, 1:3:6, visualization by bromine vapors.

N-(6-Phenanthridinyl)-1,2,3,4-tetrahydrophthalazine-1,4-dione (II). A solution of 2.09 g (10 mmoles) compound I in 100 ml benzene was dissolved with boiling, then 3.38 ml (24 mmoles) triethylamine and 1.44 ml (10 mmoles) phthaloyl chloride were successively added and a precipitate fell out of solution. The reaction mixture was heated for 30 more minutes (~100°C), then cooled down to 20°C. The residue was filtered off, washed with water to remove the triethylamine hydrochloride, dried, filtered, and recrystallized.

5-Carbethoxy-1,2,4-triazolo[4,3-*f*]phenanthridine (III). A solution of 2.09 g (10 mmoles) hydrazidine I in 20 ml diethyloxalate was boiled for 40 min (monitored by TLC). The solution was cooled down to 20°C; the precipitate was filtered off, dried, and recrystallized.

1-(6-Phenanthridinyl)-4-(*p*-tolyl)semicarbazide (IV) and 1-(6-Phenanthridinyl)-4-allylthiosemicarbazide (V). A solution of 2.09 g (10 mmoles) of compound I in 100 ml absolute benzene was dissolved with boiling and then 1.21 ml (10 mmoles) *p*-tolylisocyanate or 0.97 ml (10 mmoles) allylisothiocyanate was added; this was boiled for 15 min (compound IV) or for 1 h in the case of compound V (monitored by TLC). The isolation procedure was similar to the procedure used for compound III.

6-Arylidenehydrazinophenanthridines (VIa-e) and N-(6-Phenanthridinyl)hydrazone Isatin (VIII). A solution of 2.09 g (10 mmoles) hydrazidine I in 50 ml 2-propanol was boiled for 2 h with 10 mmoles of the appropriate carbonyl compound; then it was cooled down to 20°C and diluted with 100 ml water. The precipitate falling out of solution was filtered off, dried, and recrystallized.

5-Aryl-1,2,4-triazolo[4,3-*f*]phenanthridines (VIIa-d). A solution of 10 mmoles hydrazone VIa-d was boiled in 30 ml nitrobenzene for 1 h (monitored by TLC), cooled down to 20°C, and diluted with 50 ml ethyl alcohol. The precipitate falling out of solution was filtered off, dried, and recrystallized.

REFERENCES

1. Yu. P. Kitaev and B. I. Buzykin, Hydrazones [in Russian], Nauka, Moscow (1974).
2. É. M. Gizatullina and V. G. Kartsev, Khim. Geterotsikl. Soedin., No. 12, 1587 (1993).
3. A. G. Mikhailovskii and V. S. Shklyaev, Khim. Geterotsikl. Soedin., No. 4, 531 (1992).
4. D. B. Rubinov, A. G. Mikhailovskii, and F. A. Lakhvich, Khim. Geterotsikl. Soedin., No. 12, 1617 (1992).
5. A. G. Mikhailovskii, Abstracts, Tenth Conference of Young Scientists on Synthesis and Investigation of Biologically Active Compounds [in Russian], Riga (1989), p. 56.
6. A. G. Mikhailovskii, T. G. Taranova, B. Ya. Syropyatov, and M. I. Vakhrin, Khim.-Farm. Zh., No. 11-12, 53 (1992).
7. A. G. Mikhailovskii, Abstracts, Tenth Young Scientists' Conference on Synthetic and Natural Physiologically Active Compounds [in Russian], Yerevan (1990), p. 84.